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08/867,612	06/02/1997	YI WANG	ALX-149	2350

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	51

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/867,612	Applicant(s) WANG ET AL.
	Examiner GAMBEL	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-14, 19-34

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-14, 19-34

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. The request for a continued prosecution application (CPA) under 37 CFR 1.53(d) filed on 5/14/03 (Paper No. 50) is acknowledged. 37 CFR 1.53(d)(1) was amended to provide that the prior application of a CPA must be: (1) a utility or plant application that was filed under 35 U.S.C. 111(a) before May 29, 2000, (2) a design application, or (3) the national stage of an international application that was filed under 35 U.S.C. 363 before May 29, 2000. See *Changes to Application Examination and Provisional Application Practice*, interim rule, 65 *Fed. Reg.* 14865, 14872 (Mar. 20, 2000), 1233 *Off. Gaz. Pat. Office* 47, 52 (Apr. 11, 2000). Since a CPA of this application is not permitted under 37 CFR 1.53(d)(1), the improper request for a CPA is being treated as a request for continued examination of this application under 37 CFR 1.114. *See id.* at 14866, 1233 *Off. Gaz. Pat. Office* at 48.

Therefore, a request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 3/17/03 (Paper No. 47) has been entered.

Claims 1-14 and 17-34 are pending and being acted upon presently

Claims 15 and 16 have been canceled previously.

2. Applicant's arguments, filed 3/17/03 (Paper No. 47), are acknowledged but are rendered moot in view of the New Grounds of Rejection set forth herein.

Given an updated search and the availability of Larrick et al. (EP 0245993) as prior art, it was deemed to set forth New Grounds of Rejection set forth herein to simplify the issues and the applicability of the prior art as it reads on treating established joint inflammation as occurring in arthritis with anti-C5 or anti-C5a antibodies at the time the invention was made.

It is noted that applicant's arguments and the examiner's rebuttal of record based upon the art of record appear to be essentially the same. The prior art of record is still applicable to the claimed invention.

3. Yet once again, applicant should amend the first line of the specification to update the status of the priority application, which is now abandoned.

4. Applicant's amendment, filed 3/17/03 (Paper No. 47), has obviated certain previous objections under 35 U.S.C. 132 because it introduced new matter into the disclosure.

Applicant's arguments, filed 3/17/03 (Paper No. 47), concerning the previous objection under 35 U.S.C. 132 because it introduced new matter into the disclosure are acknowledged but would not be found persuasive for the reasons of record. However, applicant's arguments are rendered moot in view of applicant's amendment, filed 3/17/03 (Paper No. 47).

The amendment, filed 11/5/01 (Paper No. 37), stands objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendments to pages 59-60 with respect to the disclosure of "the ability of the 5G1.1 antibody to bind to both the alpha and beta chains of C5" do not appear to have adequate written description in the application as-filed.

Applicant's arguments, filed 3/17/03 (Paper No. 47), have been fully considered but are not found convincing.

Applicant argues in conjunction with In re Reynolds, 170 USPQ 94 (CCPA), In re Smythe,178 USPQ 2179 (CCPA 1973) and In re Robertson, 49 USPQ 1949, 1950-51 (Fed. Cir. 1999) to support the assertion that an application may later be amended to recite the function, theory or advantage of a device without introducing prohibited new matter. Therefore, applicant asserts that the retained matter in the 11/5/01 amendment to specification related to the ability of the 5G1.1 antibody to bind to both the alpha and beta chains of C5 as this language merely recites an inherent property of the 5G1.1 antibody and does not add new matter to the specification.

Each case must be decided on it own facts The issue here is whether the application as filed clearly conveyed to those skilled in the art that applicant has invented or more particularly with respect to the current objection, attempting to disclose.

Applicant is directed to In re Davies and Hopkins 177 USPQ 381, 385 (CCPA 1973), which provides for applicant to refile their application and incorporating a discussed of the inherent properties while retaining the effective date of the application through § 120.

This is consistent with applicant's reference to MPEP 2163.07(a) and Jewish Hospital v. St. Louis v. Idexx Laboratories, 42 USPQ2d 1720, 1723 (D. Maine 1996).

Again applicant is required to review the objected amendment to the specification and either cancel the new matter in the reply to this Office Action or provide sufficient direction to the written description for these amendments to the application as filed.

The specification does not provide sufficient blazemarks nor direction for the above-mentioned amendment on pages 59-60 of the instant specification. The instant specification now discloses limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to delete the new matter in the response to this Office Action.

Applicant's arguments are not found persuasive.

5. Claims 19-34 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed: "which binds the alpha chain of C5".

Applicant's arguments, filed 3/17/03 (Paper No. 47), have been fully considered but are not found convincing essentially for the reasons of record.

Again, applicant directs written support to the amendatory material to pages 59-60 of the specification, filed 11/5/01 (Paper No. 37) (See Appendix D) for the written description for the above-mentioned "limitation".

Applicant's arguments and the examiner's rebuttal are essentially the same as addressed above and of record.

The following of record is reiterated for applicant's convenience.

The disclosure of anti-C5 antibodies as C5 blockers does not provide sufficient written description for an antibody "which binds the alpha chain of C5".

In contrast, the instant claims appear to set forth a new subgenus by reciting However, the disclosure of anti-C5 antibodies as C5 blockers does not provide sufficient written description for an antibody "which binds the alpha chain of C5".

In contrast, the instant claims appear to set forth a new subgenus by reciting an antibody "which binds the alpha chain of C5", which, in turn, encompasses C5-specificities not disclosed in the specification as filed.

Applicant's reliance on a generic disclosure and possibly a single species does not provide sufficient direction and guidance to the "claimed limitations" having the features currently claimed

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. In re Smith 173 USPQ 679, 683 (CCPA 1972). See MPEP 2163.05(b).

Therefore even the reliance on the inherent properties of the specific 5G1.1 antibody species to bind both the alpha and beta chains of the human C5 protein does not provide adequate written description to support the current claims drawn to methods which employ antibodies that bind only the alpha chain of human C5.

The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Applicant is claiming a subgenus not supported by the specification as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action
Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.

Applicant's arguments are not found persuasive.

6. Claim 18 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 lack proper antecedent basis, given that claim 18 depends upon itself.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-10, 14, 17-28 and 32-33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Larrick et al. (EP 0245993) (see entire document).

Larrick et al. teach antibodies, including monoclonal antibodies and fragments thereof (e.g. pages 3-4 and Claims) that bind C5a and DES-ARG74-C5a which bind human complement component C5a which are particularly useful for treating conditions associated with or caused by injurious complement activation, including chronic autoimmune diseases such as rheumatoid arthritis (see entire document, including page 5, paragraph 1 of the specification, Abstract and Claims).

Larrick et al. teach that the anti-human C5a antibodies bind with an affinity of at least 10^8 liters/mole (page 3, paragraph) and are able to neutralize C5a, including inhibition of binding regardless of the particular mechanism involved wherein the antibody affects the biological activity of human C5a (page 4, paragraphs 12-13).

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

Although the reference does not disclose all of the claimed properties encompassed by the instant claims per se (e.g. see instant claims 3-10, 14, 20-28, 32) per se, given the properties of the referenced anti-human C5a antibodies to inhibit a chronic autoimmune disease such as rheumatoid arthritis and that such anti-human C5a antibodies to neutralize adverse C5a-mediated mechanisms; the claimed functional limitations would be inherent properties of the referenced human C5a-specific antibodies to treat rheumatoid arthritis.

It is noted that Larrick et al. teach various assays and properties associated with testing neutralizing anti-C5a antibodies (e.g. see pages 4-5 and Examples).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat rheumatoid arthritis with neutralizing anti-human C5a antibodies.

10. Claims 1-14 and 17 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Sims et al. (U.S. Patent No. 5,635,178) for the reasons of record set forth in Paper No. 38/44/49.

Sims et al. teach methods of inhibiting platelet or endothelial cell activation by complement proteins comprising the administration of an antibody which specifically binds to a component forming the C5b-9 complex, including effective amounts to inhibit disorders such as arthritis (see entire document, including Claims 1-3). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations encompassing properties of the active ingredient in the claims methods would be inherent properties of the claim methods to treat rheumatoid arthritis with antibodies that binds to a component forming the C5b-9 complex.

Applicant's arguments, filed 5/13/03 (Paper No. 47), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper Nos. 38/44/49.

Applicant argues in conjunction with certain legal citations that the identical invention must be shown in as complete detail as is contained in the ... claim and anticipation cannot be predicated on teachings that are vague or based on conjecture or mere conjecture as to the characteristics.

Again applicant essentially asserts that Sims et al. is limited to teaching antibodies against P18, antibodies to C7 and antibodies to C9 and that Sims et al. does not teach antibodies specific for C5.

Again applicant asserts that nowhere does Sims et al. teach antibodies specific against C5 or a method for the treatment of established joint inflammation comprising administering a composition comprising an antibody specific against C5.

Even assuming arguendo that the C5 antibodies utilized in the instant invention did somehow fall within the broad, applicant asserts that the generic claims of Sims et al. (which applicant maintain is not the case), do not invariably anticipate a claim to a species within the genus.

In contrast to applicant's assertions, Sims et al. claims methods and compositions comprising antibodies that specifically bind a component of the C5b-9 complex (see Claims 1-5). Given that C5b is a component of the C5b-9 complex, the claimed methods comprising antibodies that specifically bind a component of the C5b-9 complex reads on the claimed antibody specificity for C5.

Rather than a genus anticipating a species, here the an antibody that bind C5b anticipates antibodies that bind C5.

In contrast to applicant's assertions, Sims et al. teach the treatment of patients with immune disorders and diseases such as rheumatoid arthritis (column 14, paragraph 2, particularly, line 28). Given the teaching of treating rheumatoid arthritis, Sims et al. Is teaching the treatment of a patient with established joint inflammation.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations encompassing properties of the active ingredient in the claims methods would be inherent properties of the claim methods to treat rheumatoid arthritis with antibodies that binds to a component forming the C5b-9 complex

Applicant's arguments are not found persuasive.

11. Claims 1-14, 17-34 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Larrick et al. (EP 0245993) in view of art known assays of testing complement as taught by Auda et al. (Rheumatol. Int. 10: 185-18, 1990; 1449), Wurzner et al. (Complement Inflamm 8: 328-340, 1991), Wang et al. (U.S. Patent No. 6,074,642) and Anderson et al. (S. Afr. Med. J. 59: 666-669, 1981).

Larrick et al. (EP 0245993) has been added to provide additional teachings of treating diseases or conditions associated with joint inflammation such as a chronic autoimmune disease such as rheumatoid arthritis with neutralizing C5a-specific antibodies.

Larrick et al. teach antibodies, including monoclonal antibodies and fragments thereof (e.g. pages 3-4 and Claims) that bind C5a and DES-ARG74-C5a which bind human complement component C5a which are particularly useful for treating conditions associated with or caused by injurious complement activation, including chronic autoimmune diseases such as rheumatoid arthritis (see entire document, including page 5, paragraph 1 of the specification, Abstract and Claims). Larrick et al. teach that the anti-human C5a antibodies bind with an affinity of at least 108 liters/mole (page 3, paragraph) and are able to neutralize C5a, including inhibition of binding regardless of the particular mechanism involved wherein the antibody affects the biological activity of human C5a (page 4, paragraphs 12-13). It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. Although the reference does not disclose all of the claimed properties encompassed by the instant claims per se (e.g. see claims 3-10, 14, 20-28, 32) per se, given the properties of the referenced anti-human C5a antibodies to inhibit a chronic autoimmune disease such as rheumatoid arthritis and that such anti-human C5a antibodies to neutralize adverse C5a-mediated mechanisms; the claimed functional limitations would be intrinsic or expected properties of the referenced human C5a-specific antibodies to treat rheumatoid arthritis.

Larrick et al. differs from the claimed invention by not disclosing monitoring the levels of C5a/C5b levels after the administration of C5/C5a-specific antibodies

However, it is noted that Larrick et al. teach various assays and properties associated with testing neutralizing anti-C5a antibodies (e.g. see pages 4-5 and Examples). Larrick et al. also teach that the dose and dosage regimen will depend mainly upon whether the antibody/antibodies is/are being administered for therapeutic or prophylactic purposes (see page 5, paragraph 5).

Auda et al. teach the measurement of complement activation products in patients with chronic rheumatic diseases, including rheumatoid arthritis by ELISA assays from serum, plasma and synovial samples (see entire document). Auda et al. Teach that the measurement of anaphylatoxins ,including C5a as well as the multimolecular complement activation protein complexes are likely to be of value in the clinical situations (see page 185, column 2, paragraph 1). As pointed out in the Discussion (e.g. see page 188, column 2, paragraph 2), complement activation is thought to have a significant role in the inflammatory response and it is assumed that the level of complement activation should parallel the degree of tissue injury. Therefore, monitoring the levels of complement activation products can provide additional information and allow predictions of clinical status.

Wurzner et al. teach various assays to test the activity of complement complexes and components, including ELISAs and complement-mediated hemolysis (See entire document).

Wang et al. teach that subject to the judgement of the physician, levels of complement activity in patients are monitored according to assays such as the cell lysis assay or measuring complement levels to determine if additional doses or higher or lower dosage levels or inhibitory C5-specific antibodies are need to achieve complement reduction in patients in need (see entire document, particularly column 20, paragraph 3 and Example 4 on columns 15-16). Although Wang et al. Is directed to the treatment of glomerulonephritis, it would have been obvious to one of ordinary skill in the art at the time the invention was made to monitor complement activity in the targeted patient population given complement antagonists in order to follow the efficacy of this treatment.

Anderson et al. Teach various assays to test the activity of complement, including chemotaxis associated with the immunological assessment of patients with rheumatoid arthritis (See entire document, including Summary, Cellular Studies, Results and Discussion).

In addition, Wang et al. teach the therapeutic effects of the anti-C5a antibody 5G1.1 of the instant application (see entire document, including Summary of the Invention, Example 7). One of ordinary skill in the art at the time the invention was made would have been motivated to substitute the 5G1.1. antibody in the methods of treating arthritis taught by Larrick et al, given its pharmaceutical effects that result in blocking the generation and activation of complement.

Given the properties of the anti-complement antibodies including anti-C5/C5a antibodies (as well as the 5G1.1 antibody taught by Wang et al.) to treat various conditions and diseases including rheumatoid arthritis, one of ordinary skill in the art would have been motivated to treat patients with established joint disease with an expectation of success at the time the invention was made. The prior art teachings of Larrick et al., Auda et al. and/or Wang et al. teach the importance and value of monitoring complement during the course of a disease or treatment of a disease. Larrick et al., Auda et al., Wurzner et al., Wang et al. All teach the art known and practiced assays, including immunoassays (e.g. cell-lysing assays) and chemotaxis assays to determine complement levels and functions at the time the invention was made by the ordinary artisan in the art. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703)-872-9306.

Phillip Gambel, PhD.
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